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AF/1635

PTO/SB/21 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

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<b>TRANSMITTAL FORM</b>  (to be used for all correspondence after initial filing)	<b>Application Number</b>	10/005,344	
	<b>Filing Date</b>	December 4, 2001	
	<b>First Named Inventor</b>	Loren J. Miraglia	
	<b>Group Art Unit</b>	1635	
	<b>Examiner Name</b>	T. Gibbs	
<b>Total Number of Pages in This Submission</b>		<b>Attorney Docket Number</b>	ISIS0052-100/ISPH-0622

ENCLOSURES (check all that apply)				
<input type="checkbox"/> Fee Transmittal Form  <input type="checkbox"/> Fee Attached  <input type="checkbox"/> Amendment / Response  <input type="checkbox"/> After Final  <input type="checkbox"/> Affidavits/declaration(s)  <input type="checkbox"/> Extension of Time Request  <input type="checkbox"/> Express Abandonment Request  <input type="checkbox"/> Information Disclosure Statement  <input type="checkbox"/> Certified Copy of Priority Document(s)  <input type="checkbox"/> Response to Missing Parts/ Incomplete Application  <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Assignment Papers (for an Application)  <input type="checkbox"/> Drawing(s)  <input type="checkbox"/> Licensing-related Papers  <input type="checkbox"/> Petition  <input type="checkbox"/> Petition to Convert to a Provisional Application  <input checked="" type="checkbox"/> Power of Attorney with Revocation and Change of Correspondence Address  <input type="checkbox"/> Terminal Disclaimer  <input type="checkbox"/> Request for Refund  <input type="checkbox"/> CD, Number of CD(s)	<input type="checkbox"/> After Allowance Communication to Group  <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences  <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)  <input type="checkbox"/> Proprietary Information  <input type="checkbox"/> Status Letter  <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):  Table A Statement Under 37 CFR 3.73(b) with executed Assignment		
<table border="1"><tr><td>Remarks</td><td></td></tr></table>			Remarks	
Remarks				

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT	
Firm or Individual name	Paul K. Legaard, Registration No. 38,534
Signature	
Date	12 JANUARY 2004

CERTIFICATE OF MAILING			
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date: 12 JANUARY 2004			
Typed or printed name	Paul K. Legaard, Registration No. 38,534		
Signature		Date	12 JANUARY 2004

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**POWER OF ATTORNEY WITH REVOCATION AND  
CHANGE OF CORRESPONDENCE ADDRESS**

I hereby revoke all previous powers of attorney or authorizations of agent given in the patents/applications identified in Table A attached hereto, and appoint

☒ Practitioners at Customer Number: 34138

as my/our attorney(s) or agent(s) to prosecute the patents/applications identified in Table A, and to transact all business in the United States Patent and Trademark Office connected therewith.

Please change the Correspondence Address for the patent applications identified in Table A to:

☒ Practitioners at Customer Number: 34138

I am the:

☐ Applicant/Inventor.

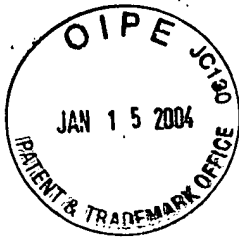
☒ Assignee of record of the entire interest. (A statement under 37 CFR 3.73(b) is enclosed.)

Respectfully submitted,  
ISIS PHARMACEUTICALS, INC.

Date: 11-6-03

By: \_\_\_\_\_

Name: B. Lynne Parshall  
Title: Executive Vice President



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**STATEMENT UNDER 37 CFR 3.73(b)**

Applicant, **ISIS Pharmaceuticals, Inc.**, a corporation, states that it is:

☒ the assignee of the entire right, title, and interest of the patent applications identified in Table A attached hereto.

The extent (by, percentage) of its ownership interest is **100%** in the patent applications identified in Table A.

☒ a copy of the pertinent assignment from the inventor(s) of the patent applications identified in Table A is enclosed herewith.

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Respectfully submitted,  
**ISIS PHARMACEUTICALS, INC.**

Date: 11-6-03

By: [Signature]  
Name: B. Lynne Parshall  
Title: Executive Vice President

## A S S I G N M E N T

WHEREAS, We, Loren J. Miraglia of Encinitas, State of California, Pamela Nero of San Diego, State of California, Mark J. Graham of San Clemente, State of California, Brett P. Monia of Encinitas, State of California, Erich Koller of Carlsbad, State of California, Ming Yi Chang of San Diego, State of California and ~~Mano~~ <sup>MUTHIAH</sup> Manoharan of Carlsbad, State of California; have invented a certain invention entitled Antisense Modulation of Human MDM2 Expression, for which we have made application for Letters Patent of the United States, said application having been filed December 4, 2001 and assigned Application No. 10/005,344; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

DOCKET NO.: ISPH-0622

PATENT

result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

DOCKET NO.: ISPH-0622

PATENT

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

DATED: May 20, 2002

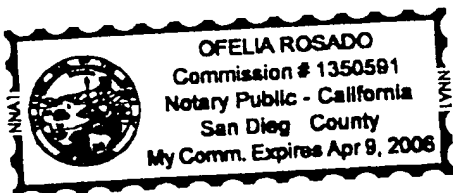
Loren J. Miraglia  
Loren J. Miraglia

State of California            )  
  ) ss.  
County of San Diego         )

On this 20<sup>th</sup> day of May, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Loren J. Miraglia, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Ofelia Rosado  
Signature of Notary



DOCKET NO.: ISPH-0622

PATENT

DATED: \_\_\_\_\_, 2002

\_\_\_\_\_  
Pamela Nero

State of California       )  
                                  ) ss.  
County of San Diego       )

On this \_\_\_\_\_ day of \_\_\_\_\_, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Pamela Nero, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

\_\_\_\_\_  
Signature of Notary

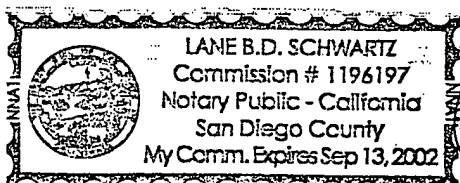
DATED: April 19, 2002

Mark J. Graham  
Mark J. Graham

State of California       )  
                                  ) ss.  
County of San Diego       )

On this 19th day of April, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Mark J. Graham, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.



Lane B.D. Schwartz  
Signature of Notary

DOCKET NO.: ISPH-0622

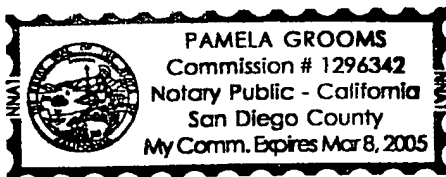
PATENT

DATED: 5/9, 2002

Brett P. Monia

State of California           )  
County of San Diego         ) ss.

On this 9th day of May 2002, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

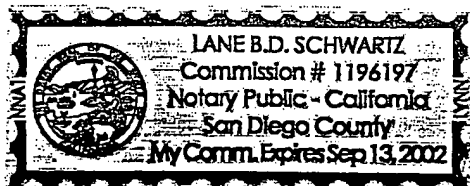
Pamela Shoom  
Signature of Notary

DATED: 4/22/02, 2002

Erich Koller

State of California           )  
County of San Diego         ) ss.

On this 22<sup>nd</sup> day of April, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Erich Koller, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Signature of Notary



DOCKET NO.: ISPH-0622

PATENT

DATED: 5-1, 2002

Ming Yi Chiang

State of California           )  
County of San Diego         ) ss.

On this 15<sup>th</sup> day of May, 2002, before me, the undersigned, a Notary Public for the State, personally appeared Ming Yi Chiang, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.




WITNESS my hand and official seal.

Signature of Notary

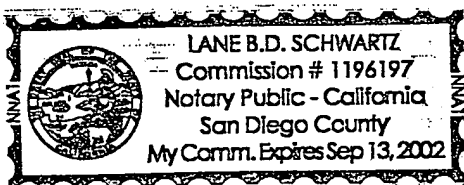
DATED: 4 / 23 , 2002

Mano Manoharan

State of California           )  
County of San Diego         ) ss.

MUTHIAH 

On this 23<sup>rd</sup> day of April, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Mano Manoharan, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Signature of Notary

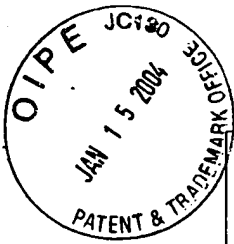
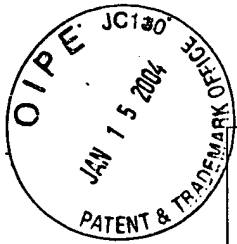
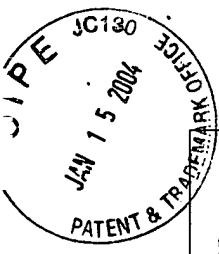


Table A

Serial No. Patent No. Docket No.	Filing Date Issue Date	Inventor(s)	Examiner	Art Unit	Title
09/200,355 6,451,524 IBIS0010-100	November 25, 1998 September 17, 2002	David J. Ecker	J. Fredman	1655	Identification of Disease Predictive Nucleic Acids
09/200,107 6,492,111 IBIS0034-100	November 25, 1998 December 10, 1998	David J. Ecker	J. Fredman	1634	<i>IN SITU</i> Binary Synthesis of Biologically Effective Molecules
10/209,761 IBIS0034-101	August 1, 2003	David J. Ecker	To Be Assigned	1634	<i>IN SITU</i> Binary Synthesis of Biologically Effective Molecules
09/076,440 6,221,587 IBIS0035-100	May 12, 1998 April 24, 2001	David J. Ecker et al.	E. Campbell	1656	Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery
09/310,667 IBIS0035-101	May 12, 1999	David J. Ecker et al.	F. Lu	1634	Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery
09/076,405 IBIS0036-100	May 12, 1998	Richard Griffey et al.	S. Broda	2123	Generation of Virtual Combinatorial Libraries of Compounds
09/753,869 IBIS0036-101	January 3, 2001	Richard Griffey et al.	M. Borin	1631	Generation of Virtual Combinatorial Libraries of Compounds
09/076,447 IBIS0037-100	May 12, 1998	Richard Griffey et al.	J. Fredman	1655	Characterization of Interactions Between Molecular Interaction Sites of RNA and Ligands Therefor

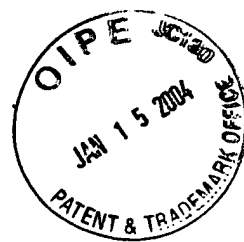


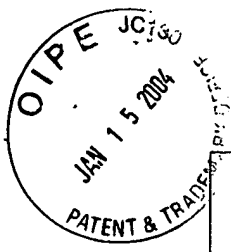
09/310,653 IBIS0037-101	May 12, 1999	Richard Griffey et al.	J. Fredman	1637	Characterization of Interactions Between Molecular Interaction Sites of RNA and Ligands Therefor
09/076,206 6,428,956 IBIS0038-100	May 12, 1998 August 6, 2001	Stanley T. Crooke et al.	S. Zitomer	1634	Mass Spectrometric Methods for Biomolecular Screening
09/260,310 6,329,146 IBIS0038-101	March 2, 1999 December 11, 2001	Stanley T. Crooke	S. Zitomer	1634	Mass Spectrometric Methods for Biomolecular Screening
09/884,317 IBIS0038-102	June 19, 2001	Stanley T. Crooke	A. Chakrabarti	1634	Mass Spectrometric Methods for Biomolecular Screening
09/884,317 IBIS0038-103	June 27, 2003	Stanley T. Crooke	To Be Determined		Mass Spectrometric Methods for Biomolecular Screening
09/076,214 IBIS0039-100	May 12, 1998	Richard H. Griffey et al.	T. Friend	1639	Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds
09/400,150 IBIS0039-101	September 21, 1999	Richard H. Griffey et al.	M. Tran	1639	Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds
60/085,092 IBIS0040-001	May 12, 1998	Stanley T. Crooke	Not applicable	Not applicable	Small Molecule Targeting Of RNA Structures
09/076,404 IBIS0040-100	May 12, 1998	David J. Ecker et al.	A. Marschel	1631	Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery
09/310,735 IBIS0040-101	May 12, 1999	David J. Ecker et al.	A. Marschel	1631	Modulation of Molecular Interaction Sites on RNA and Other Biomolecules



10/104,949 IBIS0040-102	March 22, 2002	David J. Ecker et al.	A. Marschel	1631	Modulation of Molecular Interaction Sites on RNA and Other Biomolecules
09/310,907 IBIS0041-100	May 12, 1999	David J. Ecker et al.	A. Marschel	1631	Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same
10/135,017 IBIS0041-101	April 24, 2002	David J. Ecker et al.	A. Marschel	1631	Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same
09/310,761 IBIS0042-100	May 12, 1999	David J. Ecker et al.	M. Schmidt	1635	Molecular Interaction Sites of Ornithine Decarboxylase RNA and Methods of Modulating the Same
60/314,236 IBIS0043-001	August 22, 2001	David J. Ecker	Not Applicable	Not Applicable	Molecular Interaction Sites of Hepatitis C Virus RNA and Methods of Modulating the Same
10/225,501 IBIS0043-100	August 19, 2002	David J. Ecker	To Be Assigned	1645	Methods for Identifying Ligand Binding Sites in a Biomolecule
60/314,251 IBIS0044-001	August 22, 2001	David J. Ecker	Not Applicable	Not Applicable	Molecular Interaction Sites of 23S Ribosomal RNA and Methods of Modulating the Same
10/224,836 IBIS0044-100	August 20, 2002	David J. Ecker	To Be Assigned	1645	Molecular Interaction Sites in 23S Ribosomal RNA and Methods of Modulating the Same
60/314,020 IBIS0045-001	August 21, 2001	David J. Ecker	Not Applicable	Not Applicable	Molecular Interaction Sites of RNase P RNA and Methods of Modulating the Same

10/223,156 IBIS0045-100	August 16, 2002	David J. Ecker	To Be Assigned	1645	Molecular Interaction Sites of RNase P RNA and Methods of Modulating the Same
60/313,890 IBIS0046-001	August 21, 2001	David J. Ecker	Not Applicable	Not Applicable	Molecular Interaction Sites in 16S Ribosomal RNA and Methods of Modulating the Same
10/223,126 IBIS0046-100	August 16, 2002	David J. Ecker	To Be Assigned	1645	Molecular Interaction Sites in 16S Ribosomal RNA and Methods of Modulating the Same
09/791,147 IBIS0047-100	February 22, 2001	Richard H. Griffey et al.	J. Riley	1637	Methods for Identifying Ligand Binding Sites in a Biomolecule
10/209,692 IBIS0047-101	July 31, 2002	Richard H. Griffey et al.	To Be Assigned	1645	Methods for Identifying Ligand Binding Sites in a Biomolecule
09/499,875 IBIS0048-100	February 8, 2000	Richard H. Griffey et al.	To Be Assigned	To Be Assigned	Optimization Of Ligand Affinity For RNA Targets Using Mass Spectrometry
09/573,479 IBIS0048-101	May 16, 2000	Richard H. Griffey et al.	To Be Assigned	To Be Assigned	Optimization of Ligand Affinity For RNA Targets Using Mass Spectrometry
09/630,122 IBIS0050-100	August 1, 2000	Elizabeth Jefferson	B. Coleman	1624	Antimicrobial Biaryl Compounds
08/924,851 IBIS0051-100	September 5, 1997	Eric Edward Swayze et al.	T. Prosthofor	1627	Amine Compounds and Combinatorial Libraries Comprising Same
60/291,459 IBIS0052-001	May 16, 2001	John McNeil	Not Applicable	Not Applicable	Multi-Paradigm Knowledge-Bases





10/150,668 IBIS0052-100	May 16, 2002	John McNeil et al.	To Be Assigned	2176	Multi-Paradigm Knowledge-Bases
09/411,748 6,429,016 IBIS0053-100	October 1, 1999 August 6, 2002	John McNeil	Patricia A. Bex	1743	System and Method for Sample Positioning in a Robotic System
10/153,327 IBIS0053-101	May 22, 2002	John McNeil	To Be Assigned	1743	System and Method for Sample Positioning in a Robotic System
10/067,017 IBIS0054-100	February 24, 2002	Michael L. Migawa	T. McKenzie	1624	Novel Pyranosyl Cytosines: Pharmaceutical Formulation and Methods
10/071,978 IBIS0055-100	February 6, 2002	Eric E. Swayze et al.	K. Habte	1624	Novel Benzimidazole Compounds
09/678,434 IBIS0056-100	October 2, 2000	John McNeil	E. Quan	1743	Self-Dispensing Storage Device
09/310,844 IBIS0058-100	May 12, 1999	David J. Ecker et al.	M. Schmidt	1635	Molecular Interaction Sites of Interleukin-2 RNA and Methods of Modulating the Same
09/499,875 IBIS0059-100	February 8, 2000	Richard Griffey et al.	M. Tran	1639	Optimization of Ligand Affinity for RNA Targets Using Mass Spectrometry
09/573,479 IBIS0059-101	May 16, 2000	Richard Griffey et al.	T. Prosthofer	1627	Optimization of Ligand Affinity for RNA Targets Using Mass Spectrometry
10/005,344 ISIS0052-100	December 4, 2001	Loren J. Miraglia et al.	T. Gibbs	1635	Antisense Modulation of Human MDM2 Expression

10/281,349 ISIS0002-105	October 25, 2002	Stanley T. Crooke	To Be Assigned	1635	Oligoribonucleotides and Ribonucleases for Cleaving RNA
10/327,805 ISIS0060-101	December 20, 2002	Brett P. Monia et al.	To Be Assigned	1635	Antisense Modulation of SMAD6 Expression

